REMARKS

Upon entry of the present amendment, claims 1, 13, and 16-29 are pending in this application. Claim 1 has been amended and new claims 18-29 have been added. The present amendments introduce no new matter.

Claim Objections

The Examiner has objected to claims 1 and 8 because more than one period was used in the claims. Claim 8 has been canceled and Applicants have amended claim 1 such that it contains one period. As such, this objection is moot and should be withdrawn.

Claim Rejection 35 USC § 112, first paragraph: Written Description

The Examiner has rejected claims 1, 2, 4, 8, 9, 11, 13-14 and 16-17 under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s) at the time the application was filed, had possession of the claimed invention. The claims are directed to encompass "cholinergic agent", which the Examiner states does not meet the written description requirement due to lacking chemical structure information. Applicants traverse the rejection with respect to the pending claims as amended and added herein.

Without acceding to the Examiner's position and in the interest of expediting prosecution, claim 1 (from which the remaining claims subject to the rejection depend) is amended to delete "cholinergic agent" and to recite "pilocarpine," which the Examiner states meets the written description provisions of 35 U.S.C. §112, first paragraph. *See*, Office Action at page 3. As such, Applicants request withdrawal of the rejection.

Claim Rejection 35 USC § 112, first paragraph: Enablement

The Examiner has rejected claims 1, 2, 4, 8, 9, 11 and 13-17 under 35 USC 112, first paragraph, because the Examiner states that the specification while being enabling for "pilocarpine" with the combination of the specific compound of formula I such as 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolidum chloride for decreasing intraocular pressure, does not provide enablement for use of "cholinergic agent" with the compound of formula I for decreasing intraocular pressure or improving ocular accommodation.

Specifically, the Examiner states that the instant compounds represented by the formula embrace compounds with substituents bearing plethora of structural cores (e.g., Q is N, O, or S) and functional groups and other groups which include variously substituted C5-C10 aryl ring or aromatic fused ring with variable ring sizes and variable heteroatoms variety of reactive functional groups. *See*, Office Action at page 6.

The Examiner also states that it is generally recognized in the art that biological compounds often react unpredictably under different circumstances and thus there is no reasonable basis for assuming that the myriad of compounds embraced by the claim language will all share the same bioactivity profile since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same (as to "a compound of formula I"). *See*, Office action at pages 6-7

Further, the Examiner says that the lack of working examples regarding the activity of the claimed compounds toward utility in humans or animals, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims. *See*, Office Action at page 7.

Applicants traverse the rejection with respect to the pending claims as amended and added herein.

As described *supra*, claim 1 (from which the remaining claims subject to the rejection depend) is amended to delete "cholinergic agent" and to recite "pilocarpine," which the Examiner states meets the enablement provisions of 35 U.S.C. §112, first paragraph. *See*, Office Action at page 3.

Claim 1 is also amended such that the compounds represented by the formula embrace compounds with the structural core Q = S. Further, Applicants have significantly amended the definitions of R^1, R^2, Z, Y, R^5, R^6, W, R^7, Rs, and M and the definitions of R^9 and R^{10} have been canceled in their entirety. That is, the claims as amended are directed to the use of specific thiazolium compounds to inhibit advanced glycation and decrease intraocular pressure.

Applicants submit that one skilled in the art reading the instant specification could readily make and use the claimed compounds of formula I in combination with pilocarpine to decrease intraocular pressure with a reasonable expectation of success. The instant specification readily describes that eye disorders which result from increased intraocular pressure, such as glaucoma, are the result of advanced glycosylation end products and that the claimed thiazolium compounds inhibit advanced glycation and thus can decrease intraocular pressure and treat the

resultant disorders such as glaucoma. *See*, specification at pages 12-13. Moreover, the instant specification provides working examples, which demonstrate significant ability of these thiazolium compounds to decrease intraocular pressure in animal models that assess ophthalmologic function. Applicants submit that one of ordinary skill in the art would readily understand that the working examples described in the specification are not limited to the compound, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)thiazolium, employed in the specific example. But rather, the skilled artisan would consider the working examples to be applicable to include the thiazolium compounds and advanced glycation inhibitors of the claimed invention. Example 12 found on page 57, line 24 of the as-filed specification describes the effect of 4,5-dimethyl-3-(2-oxo-2-phenylethyl)thiazolium on the outflow facility in primates. The results of this study show a statistically significant increase in baseline outflow in the treated vs. control eye and indicate sustained improvement in pilocarpine-stimulated facility as shown in Table 1. Figure 2 as discussed on page 47, lines 1-20 shows effects of the route of administration on outflow facility. Examples 13 and 14 found on page 58 demonstrate successful penetration through an intact cornea in rabbits and monkeys.

Armed with the above described teachings, as well as, the information provided in the specification regarding how to prepare the compounds, how to administer the compounds, formulation, and dosage (*See*, for example, page 38, line 6 - page 49, line 5 and Examples 1-6, 8-9, 12-17 of the as-filed specification), those skilled in the art would readily be able to carry out the invention as now claimed without undue experimentation.

In view of the above, Applicants respectively request reconsideration and withdrawal of the rejection.

Claim Rejections 35 USC § 112, second paragraph

The Examiner has rejected claims 1, 2, 4, 8, 9, 11, and 13-17 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that the specification does not define the term "improving ocular accommodation" in claim 1. Applicants traverse the rejection with respect to the pending claims as amended and added herein.

Applicants submit that the instant specification at page 47 defines the term "improving ocular accommodation" as "the process of effecting refractive changes in the shape of the lens" and as such this terms is not vague or indefinite. However, in the interest of expediting

prosecution, claim 1 (from which the remaining claims subject to the rejection depend) is amended to delete "improving ocular accommodation". Accordingly, this rejection is moot and should be withdrawn.

CONCLUSION

On the basis of the foregoing amendment and remarks, Applicants respectfully submit that the pending claims are in condition for allowance and a Notice of Allowance for the pending claims is respectfully requested. If there are any questions regarding this application that can be handled in a phone conference with Applicants' Attorneys, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

Ivor R. Elrifi, Reg. No. 39,529
Matthew Pavao, Reg. No. 50,572
Attorneys for Applicants
c/o MINTZ, LEVIN
Tel: (617) 542-6000
Fax: (617) 542-2241
Customer No.: 30623

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